# Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

**Sponsor:** Pfizer Inc.

**Medicine(s) Studied:** DAURISMO® (glasdegib)

**Protocol Number:** B1371019

**Dates of Study:** Intensive Treatment Group: 20 April 2018 to 01 February 2021, with data collected to 11 November 2021;
Non-Intensive Treatment Group: 18 June 2018 to 05 June 2020, with data collected to 17 January 2022

**Title of this Study:** Study of Glasdegib with Intensive or Standard Chemotherapy in Patients with Untreated Acute Myeloid Leukemia

[A Randomized (1:1), Double-Blind, Multi-Center, Placebo Controlled Study Evaluating Intensive Chemotherapy With or Without Glasdegib (PF-04449913) or Azacitidine (AZA) With or Without Glasdegib in Patients With Previously Untreated Acute Myeloid Leukemia]

**Date(s) of this Report:** 13 September 2022

# – Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

# Why was this study done?

## What is acute myeloid leukemia?

Acute myeloid leukemia is also known as AML and is a common cancer of the blood. AML starts when myeloid cells in the bone marrow begin to grow out of control. The bone marrow is the soft inner part of certain bones, and it is where new blood cells are made. The myeloid cells would normally develop into red blood cells, certain types of white blood cells, and platelets. Red blood cells are used to carry oxygen from the lungs around the body to where it is needed. These red blood cells also take carbon dioxide back to the lungs so it can be breathed out. White blood cells are used to fight infections. Platelets help to stop bleeding when blood vessels are damaged. While AML starts in the bone marrow, it often spreads to other areas of the body.

## What is glasdegib?

This study investigated the use of glasdegib, which is new type of treatment known as a hedgehog or smoothened (SMO) inhibitors. Glasdegib is designed to reduce or stop the growth of cancer cells. At the time this study began, glasdegib was an investigational (or experimental) drug. An investigational drug is one that is not approved for sale in the country where it is being used. During this study, the US Food and Drug Administration (FDA) gave their approval for glasdegib to be used with low dose cytarabine to treat newly diagnosed AML. This was in November 2018. The European Medicines Agency (EMA) gave their approval in June 2020. Glasdegib is sold in these countries as DAURISMO®.

The other treatments used in this study are cytarabine, daunorubicin, and azacitidine. These are all licensed cancer treatments for AML and are often described as chemotherapy.

## What was the purpose of this study?

The purpose of this research study is to compare the effects of the study drug, glasdegib, with a placebo, to find out how well glasdegib worked in combination with chemotherapy to help participants live longer. Two different types of chemotherapy were tested in this study:

- Intensive chemotherapy with cytarabine and daunorubicin. These treatments are often used to treat patients with AML in the US and Europe, but this type of chemotherapy is quite aggressive. This means the medicines are strong and quite toxic and not all patients with AML are suitable for this intensive chemotherapy.
- Standard chemotherapy with azacitidine. This is one of the medicines used to treating patients with AML in the US and Europe if the patient is not suitable for intensive chemotherapy.

**Researchers wanted to know:**

**Did the participants taking glasdegib with chemotherapy live longer compared to participants not taking glasdegib?**

# What happened during the study?

## How was the study done?

This study included participants with AML who had not previously been treated for their cancer. The participants were split into 2 groups:

- An Intensive Treatment Group – this included participants who were suitable for intensive chemotherapy with cytarabine and daunorubicin
- A Non-Intensive Treatment Group – this included participants who were not suitable for intensive chemotherapy and who were given standard chemotherapy with azacitidine.

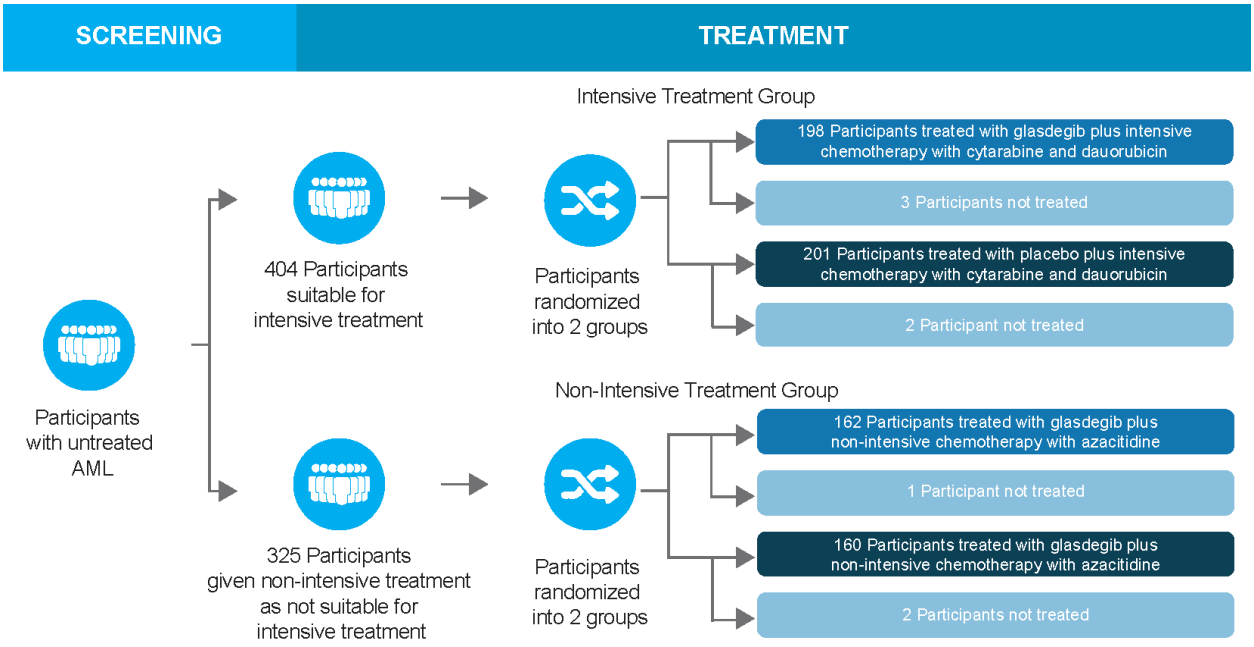
The researchers then tested glasdegib on each group of study participants to find out if study participants taking glasdegib plus chemotherapy lived longer compared to study participants given placebo plus chemotherapy. A placebo does not have any medicine in it, but it looks just like the study medication. Participants took glasdegib or placebo tablets once a day and this treatment could be continued for up to 2 years. Participants received intensive or non-intensive chemotherapy, and this was given

according to the manufacturer's recommendations. Participants who stopped treatment in this study were followed to check on their health.

Researchers compared the results of study participants taking glasdegib plus chemotherapy to the results of study participants taking placebo plus chemotherapy. The study participants and researchers did not know who took glasdegib and who took the placebo. This is known as a "blinded" study. This study was double-blinded, which means nobody knew who was taking what treatment during the study. Study participants were assigned to each group by chance alone.

The study plan is shown in Figure 1.

**Figure 1: Study Plan**




## Where did this study take place?

For the Intensive Treatment Group, the Sponsor ran this study at 94 locations in 20 countries in North America, Central America, Europe, Asia, and Australia. For the Non-Intensive Treatment Group, the Sponsor ran this study at 83 locations in 21 countries in North America, Central America, Europe, Asia, and Australia.

## When did this study take place?

For the Intensive Treatment Group, the study began 20 April 2018 and ended 01 February 2021, with data collected up to 11 November 2021. For the Non-Intensive Treatment Group, the study began 18 June 2018 and ended 05 June 2020, with data collected up to 17 January 2022.

## Who participated in this study?

The study included participants who had AML but who had not previously been treated for their cancer.

In the Intensive Treatment Group,

- A total of 236 men participated
- A total of 168 women participated
- All participants were between the ages of 19 and 86 years

In the Non-Intensive Treatment Group,

- A total of 186 men participated
- A total of 139 women participated
- All participants were between the ages of 47 and 94 years

Participants were to be treated until their cancer got worse, they experienced unacceptable toxicity, they left the study, or the participant died.

In the Intensive Treatment Group, of the 399 participants who started the study and received treatment, 390 participants stopped taking the study treatment. All 399 participants left before the study was over by their choice or a doctor decided it was best for a participant to stop being in the study, or because they passed away, or the Sponsor closed the study. Most participants left the study because they died.

In the Non-Intensive Treatment Group, of the 322 participants who started the study and received treatment, 306 participants stopped taking the study treatment. There

were 305 participants who left before the study was over by their choice or a doctor decided it was best for a participant to stop being in the study, or because they passed away, or the Sponsor closed the study. Most participants left the study because they died or because the Sponsor closed the study. There are 7 participants who are continuing in this study from the Non-Intensive Treatment Group.

### How long did the study last?

In the Intensive Treatment Group, study participants were in the study for up to 2 years and 9 months, with data collected for around 3 years and 7 months. In the Non-Intensive Treatment Group, study participants were in the study for up to 1 year and 11 months, with data collected for around 3 years and 7 months.

The researchers stopped participants in the Intensive Treatment Group from continuing in the study after an early analysis of the data in 2020. They did this because they found there was no difference between the participants who were treated with glasdegib plus intensive chemotherapy and participants who were treated with placebo plus intensive chemotherapy.

For the Intensive Treatment Group, the Sponsor began reviewing the information collected up to November 2021 and closed this part of the study early. The Sponsor then created a report of the results. For the Non-Intensive Treatment Group, the Sponsor began reviewing the information collected up to January 2022. The Sponsor then created a report of the results. This is a summary of the reports for the Intensive Treatment Group and the Non-Intensive Treatment Group. At the time of writing, there are 7 participants from the Non-Intensive Treatment Group who are continuing in this study.

## What were the results of the study?

### Did the participants taking glasdegib with chemotherapy live longer compared to participants not taking glasdegib?

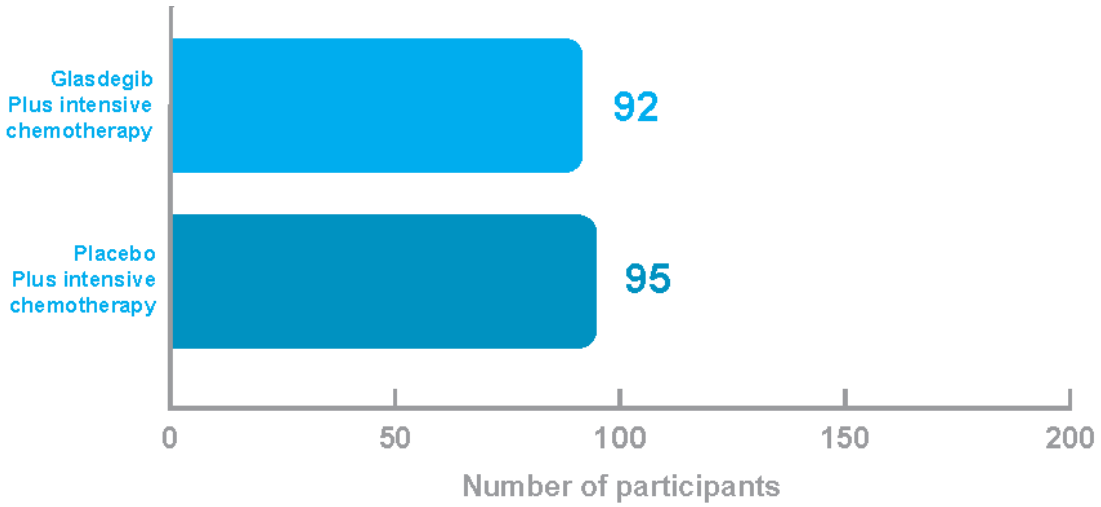
To answer this question, researchers looked at the overall survival of participants in the study. Overall survival is the number of participants in a treatment group who are

alive at the end of a study. Researchers calculated this by comparing the number of participants who were alive in the glasdegib plus chemotherapy group with the number of participants who were alive in the placebo plus chemotherapy.

## What was the overall survival of participants taking glasdegib compared to participants taking placebo in the Intensive Treatment Group?

At the end of the study, 92 out of the 201 (46%) participants who were originally allocated treatment with glasdegib plus intensive chemotherapy were known to be alive. There were 95 out of the 203 (47%) participants who were originally allocated treatment with placebo plus intensive chemotherapy known to be alive. The researchers concluded that the results were similar between the glasdegib and placebo groups as shown in Figure 2.

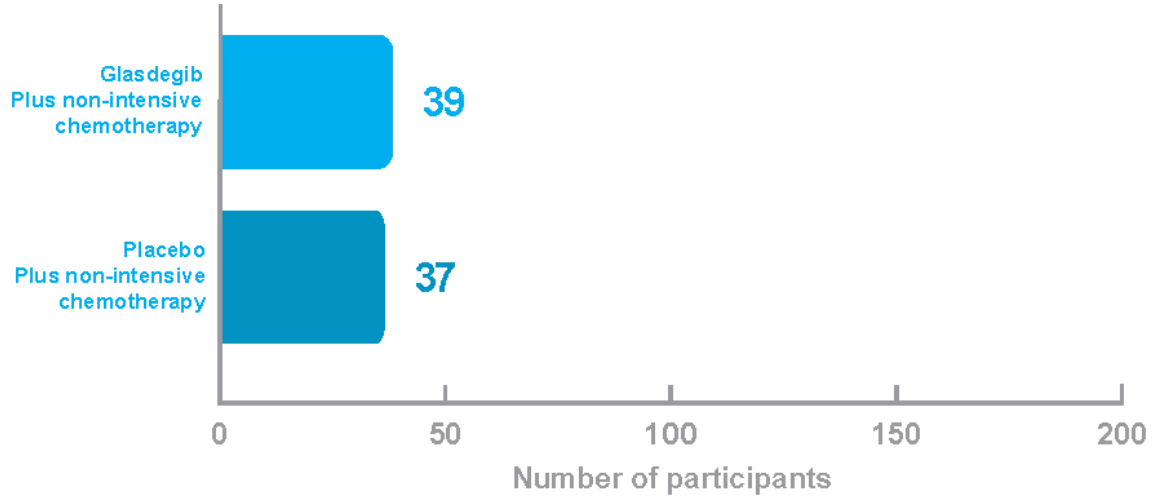
**Figure 2. Intensive Treatment Group: Participants Who Were Alive at the End of the Study**



## What was the overall survival of participants taking glasdegib compared to participants taking placebo in the Non-Intensive Treatment Group?

At the end of the study, 39 out of the 163 (24%) participants who were originally allocated treatment with glasdegib plus standard chemotherapy were known to be alive. There were 37 out of the 162 (23%) participants who were originally allocated treatment with placebo plus standard chemotherapy known to be alive. The researchers concluded that the results were similar between the glasdegib and placebo groups as shown in Figure 3.

**Figure 3. Non-Intensive Treatment Group: Participants Who Were Alive at the End of the Study**




Based on these results, the researchers have decided that the study results are likely the result of chance. This means the study did not show that one treatment was better than another at helping participants with untreated AML live longer. Participants in both the glasdegib and placebo groups had a similar amount of survival.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study. Other studies with glasdegib may have different results.

# What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

In the Intensive Treatment Group, 394 out of 399 (99%) participants in this study had at least 1 medical problem. A total of 41 (10%) participants left the study because of medical problems. In the Non-Intensive Treatment Group, 319 out of 322 (99%) participants in this study had at least 1 medical problem. A total of 108 (34%) participants left the study because of medical problems.

The most common medical problems – those reported by at least 30% of participants – are described below.

Below are instructions on how to read Table 1 and 2. These instructions can also be used for Table 3 and 4, which lists serious medical problems.

### Instructions for Understanding Table 1 and 2.

- The **1st** column of Table 1 and 2 lists medical problems that were commonly reported during the study. All medical problems reported by at least 30% of participants are listed.
- The **2nd** column tells how many of the participants taking the glasdegib plus intensive or standard chemotherapy reported each medical problem. Next to this number is the percentage of the participants taking glasdegib plus intensive or standard chemotherapy who reported the medical problem.

- The **3rd** column tells how many of the participants taking placebo plus intensive or standard chemotherapy reported each medical problem. Next to this number is the percentage of the participants taking placebo plus intensive or standard chemotherapy who reported the medical problem.
- Using these instructions, you can see that:
    - In the Intensive Treatment Group, 110 out of the 198 (56%) participants taking glasdegib plus intensive chemotherapy reported nausea. A total of 108 out of the 201 (54%) participants taking a placebo plus intensive chemotherapy reported nausea.
    - In the Non-Intensive Treatment Group, 75 out of the 162 (46%) participants taking glasdegib plus standard chemotherapy reported low numbers of red blood cells in the blood. A total of 73 out of the 160 (46%) participants taking placebo plus standard chemotherapy reported low numbers of red blood cells in the blood

| Table 1. Intensive Treatment Group: Commonly reported medical problems by study participants | | |
|---|---|---|
| **Medical problem** | **Glasdegib plus Intensive Chemotherapy (198 Participants)** | **Placebo plus Intensive Chemotherapy (201 Participants)** |
| **Nausea** | 110 out of 198 participants (56%) | 108 out of 201 participants (54%) |
| **Low numbers of neutrophils, a type of white blood cell, in the blood plus fever** | 106 out of 198 participants (54%) | 107 out of 201 participants (53%) |
| **Low numbers of red blood cells in the blood** | 106 out of 198 participants (54%) | 101 out of 201 participants (50%) |
| **Diarrhea** | 98 out of 198 participants (49%) | 88 out of 201 participants (44%) |
| **Fever** | 83 out of 198 participants (42%) | 87 out of 201 participants (43%) |
| **Low levels of potassium in the blood** | 76 out of 198 participants (38%) | 84 out of 201 participants (42%) |
| **Low numbers of platelets in the blood** | 80 out of 198 participants (40%) | 76 out of 201 participants (38%) |
| **Constipated** | 71 out of 198 participants (36%) | 61 out of 201 participants (30%) |
| **Low numbers of white blood cells in the blood** | 65 out of 198 participants (33%) | 54 out of 201 participants (27%) |

| Table 2. Non-Intensive Treatment Group: Commonly reported medical problems by study participants | | |
|---|---|---|
| **Medical problem** | **Glasdegib plus Standard Chemotherapy (162 Participants)** | **Placebo plus Standard Chemotherapy (160 Participants)** |
| **Low numbers of red blood cells in the blood** | 75 out of 162 participants (46%) | 73 out of 160 participants (46%) |
| **Constipation** | 59 out of 162 participants (36%) | 52 out of 160 participants (33%) |
| **Nausea** | 58 out of 162 participants (36%) | 44 out of 160 participants (28%) |
| **Pneumonia** | 43 out of 162 participants (27%) | 48 out of 160 participants (30%) |
| **Fever** | 48 out of 162 participants (30%) | 42 out of 160 participants (26%) |

## Did study participants have any serious medical problems?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

In the Intensive Treatment Group, 135 participants (34%, or 135 out of 399 participants) had serious medical problems.

- There were 86 out of 198 (43%) participants taking glasdegib plus intensive chemotherapy who had serious medical problems.
    - Of these, 41 out of 198 (21%) had serious medical problems considered related to treatment.

- There were 92 out of 201 (46%) participants taking placebo plus intensive chemotherapy who had serious medical problems.
    - Of these, 43 out of 201 (21%) had serious medical problems considered related to treatment.

Table 3 lists all serious medical problems reported by at least 5% of participants in the Intensive Treatment Group.

**Table 3. Intensive Treatment Group: Commonly reported serious medical problems**

| Serious medical problem | Glasdegib plus Intensive Chemotherapy (198 Participants) | Placebo plus Intensive Chemotherapy (201 Participants) |
|---|---|---|
| **Low numbers of neutrophils, a type of white blood cell, in the blood plus fever** | 18 out of 198 participants (9%) | 17 out of 201 participants (8%) |
| **Blood poisoning (sepsis)** | 15 out of 198 participants (8%) | 13 out of 201 participants (6%) |
| **Pneumonia** | 15 out of 198 participants (8%) | 11 out of 201 participants (5%) |
| **Abnormal heart function test** | 13 out of 198 participants (7%) | 8 out of 201 participants (4%) |

In the Non-Intensive Treatment Group, 241 participants (75%, or 241 out of 322 participants) had serious medical problems.

- There were 117 out of 162 (72%) participants taking glasdegib plus standard chemotherapy who had serious medical problems.
    - Of these, 45 out of 162 (28%) had serious medical problems considered related to treatment.

- There were 124 out of 160 (78%) participants taking placebo plus standard chemotherapy who had serious medical problems.
    - Of these, 37 out of 160 (23%) had serious medical problems considered related to treatment.

Table 4 lists all serious medical problems reported by at least 5% of participants in the Non-Intensive Treatment Group.

**Table 4. Non-Intensive Treatment Group: Commonly reported serious medical problems by study participants**

| Serious medical problem | Glasdegib plus Standard Chemotherapy (162 Participants) | Placebo plus Standard Chemotherapy (160 Participants) |
|---|---|---|
| **Pneumonia** | 29 out of 162 participants (18%) | 36 out of 160 participants (23%) |
| **Low numbers of neutrophils, a type of white blood cell, in the blood plus fever** | 24 out of 162 participants (15%) | 20 out of 160 participants (13%) |
| **Acute myeloid leukemia (AML) worsened** | 14 out of 162 participants (9%) | 22 out of 160 participants (14%) |
| **Blood poisoning (sepsis)** | 14 out of 162 participants (9%) | 10 out of 160 participants (6%) |
| **Urine infection** | 9 out of 162 participants (6%) | 4 out of 160 participants (3%) |
| **Fever** | 11 out of 162 participants (7%) | 11 out of 160 participants (7%) |

In the Intensive Treatment group, 90 (45%) participants who were taking glasdegib plus intensive chemotherapy died during the study. There were 88 (43%) participants who took placebo plus intensive chemotherapy who died. The most common cause of death was the AML worsening. This was reported in 52 (26%) participants taking glasdegib plus intensive chemotherapy and 49 (24%) participants taking placebo plus intensive chemotherapy.

In the Non-Intensive Treatment Group, 117 (72%) participants who were taking glasdegib plus standard chemotherapy died during the study. There were 113 (70%) participants who were taking placebo plus standard chemotherapy who died. The most common cause of death was the AML worsening. This was reported in 69 (42%) participants taking glasdegib plus standard chemotherapy and 68 (42%) participants taking placebo plus standard chemotherapy.

## Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

The full scientific report of this study is available online at:

| | |
|---|---|
| www.clinicaltrials.gov | Use the study identifier **NCT03416179** |
| www.clinicaltrialsregister.eu | Use the study identifier **2017-002822-19** |
| www.pfizer.com/research/research_clinical_trials/trial_results | Use the protocol number **B1371019** |

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!